

NK-cells in placenta of female patients with type 1 diabetes mellitus

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Placenta is a temporary organ that performs multiple functions to provide a normal course of the intrauterine development of the child. However, immune interactions in placenta are not well understood. Since women with type 1 diabetes mellitus have a greater risk of adverse pregnancy outcomes due to aberrant immunological adaptation, the study of immunological interactions in placenta of these women is of particular interest. In this study a comparative analysis of the age-related expression parameters of marker of NK-cells (CD57) in placenta in patients with type 1 diabetes mellitus was performed. The current study revealed differences in the expression parameters of NK-cells marker between two age subgroups of the patients and compared to healthy controls. The results indicate the high significance of inflammatory markers in women with type 1 diabetes mellitus for assessing the course of pregnancy and the possible development of somatic pathology in newborns, especially from older women.

Keywords: type 1 diabetes mellitus, T1DM, pregnancy, NK-cells, autoimmunity in pregnancy.

Introduction

Placenta is a temporary organ that connects a developing fetus through the umbilical cord with uterine and provides assimilation of nutrients and oxygen, thermoregulation, and removal of metabolic products through maternal bloodstream. Moreover, placenta produces a number of hormones that affect the pregnancy course. However, many issues related to the placental barrier, in particular, immune interactions, remain unknown.

According to the recent data, pregnancy in women with type 1 diabetes mellitus (T1DM) is associated with risks of premature birth, preeclampsia, macrosomia, fetal death, heart and kidney malformations, however, glycemic control and pregravid preparation can reduce the frequency of fetal death and malformations [1].

Different phases of pregnancy are pro- and anti-inflammatory [2]. Thus, the phase of rapid fetal growth and development is anti-inflammatory, while the phases of implantation and childbirth are pro-inflammatory. Currently, it is known that tolerance of the maternal organism to the fetus is caused by modulation of the immune system [3]. Since

women with T1DM have a greater risk of adverse pregnancy outcomes due to aberrant immunological adaptation (such as changes in the number of leukocytes, the increased ratio of Th1/Th2, increased expression of CD335 in NK-cells, enhanced activation of intermediate and non-classical monocytes [4]), the study of immunological interactions in placenta of women with T1DM is of particular interest.

The aim of our study was a comparative analysis of the age-related expression parameters of marker of NK-cells (CD57) in placenta in patients with T1DM. The villous chorion was the object of the study, since, due to the structural features, it plays the most important role in the implementation of metabolic processes between maternal and fetal bloodstreams.

Materials and methods

The samples of 80 placentas at 36–40 gestation weeks were chosen for our study. All samples were obtained at the Maternity department of the D. O. Ott Research Institute of Obstetrics, Gynecology and Reproductology (St. Petersburg, Russia) from primiparous and multiparous women aged from 19 to 40 years. For control group the samples from women without T1DM, T2DM and gestational diabetes were obtained. According to previous studies, in pregnant women who are over 28 y. o., in most cases, involutive and dystrophic changes in placenta are observed [5]. In this regard, the samples were divided into groups (table) from 19 to 28 y. o. (inclusive) and older than 28 y. o. to 40 y. o. (inclusive).

Table. Information about groups dividing

	Group	Mean age, years	Number of samples	Designation
Control	Primiparous ≤ 28	23.6 ± 1.39	n = 10	CPY
	Primiparous > 28	34.0 ± 2.42	n = 10	CPO
	Multiparous ≤ 28	24.11 ± 1.73	n = 10	CMY
	Multiparous > 28	35.3 ± 3.15	n = 10	CMO
T1DM	Primiparous ≤ 28	24.67 ± 0.97	n = 10	DPY
	Primiparous > 28	33.0 ± 2.03	n = 10	DPO
	Multiparous ≤ 28	25.48 ± 1.83	n = 10	DMY
	Multiparous > 28	35.23 ± 1.67	n = 10	DMO

The histological sections were prepared according to the standard protocol for FFPE tissues. For immunohistochemical staining, sections were placed on glass slides coated with a film of poly-L-lysine (Sigma). CD57 (1:50, Novocastra) primary monoclonal antibodies were used. A universal kit containing biotinylated secondary antibodies was used (ABC-kit, Novocastra). Morphometric analysis was performed using “VideoTest Morphologia 5.0” software. In each case, 5 fields of view were analyzed at a magnification of 400. The relative area (RA) and the optical density (OD) of expression were taken as the estimated parameters. These parameters reflect the intensity of synthesis or accumulation of the signal molecules. Statistical analysis was carried out using Statistica 6.0.

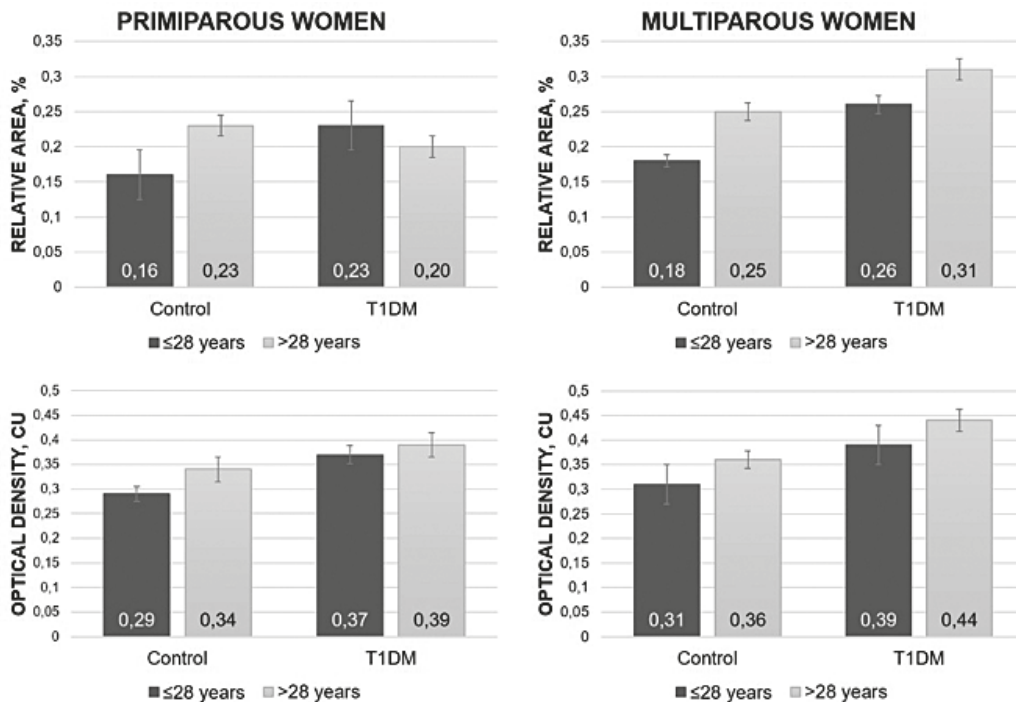


Fig. The relative area and the optical density of CD57 expression in placentas

Results

In all cases the delivery occurred at a gestational age of 37–40 weeks. The body weight of newborns in women in the control group was from 3040 to 3880 g (mean weight 3488 ± 126 g), in the T1DM group — from 3180 to 4300 g (mean weight 3690 ± 260 g). According to the mass and height parameters of newborns, no significant differences were found. The lowest Apgar score in the groups studies (6 points) was observed in the subgroup of older women in the T1DM group. In addition, postpartum jaundice was detected in 35 % of newborns of mothers with T1DM. The expression of the NK-cells marker in the chorionic villi was weak in all studied groups. However, from the data obtained, it can be concluded that NK-cells are present in the placentas of women with T1DM in a greater amount than in control group. In the subgroups of multiparous women, a decrease in the RA of CD57 was found in the subgroup of older reproductive age compared with the younger one in T1DM group (figure).

Conclusion

The current study revealed differences in the expression parameters of NK-cells marker between patients with T1DM and healthy patients. The signaling molecules and cytokines produced by immune cells play a key role in the development of pathological conditions that occur during pregnancy. Our study confirms the presence of ongo-

ing changes in the uterus-placenta system in T1DM patients. In our previous study we showed that NK-cells as well as cytotoxic T-cells has a great impact in development of gestosis [6], and women with T1DM have a significant greater incidence of gestosis than a control group. The results of the current study indicate the high epidemiological and research significance of inflammatory markers for assessing the course of pregnancy and the possible development of somatic pathology in newborns, especially from older women.

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